

Bubble formation occurs in insulin pumps in response to changes in ambient temperature and atmospheric pressure but not as a result of vibration

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ABSTRACT

Introduction: Bubble formation in insulin pump giving sets is a common problem. We studied change in temperature, change in atmospheric pressure, and vibration as potential mechanisms of bubble formation.

Methods: 5 Animas 2020 pumps with 2 mL cartridges and Inset II infusion systems, 5 Medtronic Paradigm pumps with 1.8 mL cartridge and Quickset and 3 Roche Accu-check pumps with 3.15 mL cartridges were used. Temperature study: insulin pumps were exposed to a temperature change from 4°C to 37°C. Pressure study: insulin pumps were taken to an altitude of 300 m. Vibration study: insulin pumps were vigorously shaken. All were observed for bubble formation.

Results: Bubble formation was observed with changes in temperature and atmospheric pressure. Bubble formation did not occur with vibration.

Discussion: Changes in insulin temperature and atmospheric pressure are common and may result in bubble formation. Vibration may distribute bubbles but does not cause bubble formation.

INTRODUCTION

At our centre, patients using insulin pump therapy frequently report bubble formation in insulin cartridges and tubing. Bubble formation is a concern to patients and families who often fear that non-delivery of insulin will result. The causes of bubble formation in insulin cartridges and tubing have not previously been studied.

Case study

A child with type 1 diabetes mellitus managed with a Medtronic Veo insulin pump lived on a remote farm where there were commonly large temperature changes through the day (10–35°C). The child travelled 10 km to school on a rough dirt tract that included a 600 m climb. The family frequently found bubbles in the insulin pump tubing and cartridge on arrival at school and were concerned about the impact of the bubbles on insulin

Key messages

- Bubble formation in insulin pumps is common and may cause anxiety for patients and families.
- Changes in ambient temperature and atmospheric pressure may result in bubble formation in insulin pumps.
- Vibration of an insulin pump does not result in bubble formation.

delivery. In our clinical practice, it is not uncommon for patients and their families to report bubble formation in insulin pump cartridges and tubing.

We studied physical factors that may be involved in bubble formation, including change in pressure, change in temperature, and vibration.

METHODS

Only mechanical equipment was used in these studies, therefore ethics approval was not sought.

Five Animas 2020 pumps with 2 mL cartridges (IR1200/2020; Animas, West Chester, Pennsylvania, USA) and Inset II infusion systems (Animas), five Medtronic Paradigm pumps with 1.8 mL cartridge and Quickset (Medtronic, Minneapolis, Minnesota, USA), and three Roche Accu-check spirit pumps with 3.15 mL cartridge (F.Hoffman-La Roche, Basel, Switzerland) and Inset II infusion sets (Animas) were used.

The cartridges were filled with aspart insulin (NovoNordisk, Bagsvaerd, Denmark) and loaded into the pumps as described in the product literature.

Temperature study

We used Henry's law to model bubble formation from saline that occurs as the temperature changes¹ (see [figure 1](#)).

Six cartridges and tubing systems (three Animas 2 mL cartridges and three Roche



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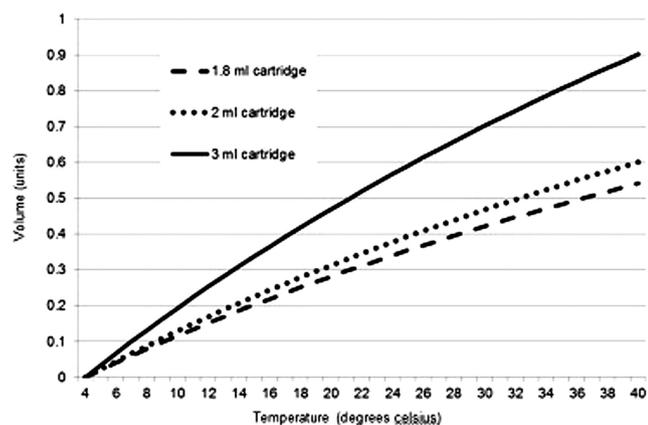


Figure 1 Mathematical modeling of bubble formation in insulin pump cartridges (3 mL solid line, 2 mL dotted line, and 1.8 mL dashed line) and lines during an increase in temperature from 4°C to 37°C. Henry's law (1) was used to graph the predicted bubble formation in insulin as the temperature changes between 4°C and 37°C.

3.15 mL cartridges) were filled with aspart insulin at 4°C. Six insulin pumps (three Animas 2020 and three Roche Accu-chek) were kept at room temperature. The insulin cartridges and tubing were taken out of the refrigerator and loaded into the insulin pumps. The insulin pumps containing the cartridges and infusion sets were placed into an oven (Thermoline Labtech, Sydney, Australia) at 37°C for 3 h. The insulin pumps and cartridges were then removed from the oven and examined for bubble formation. The experiment was repeated five times.

Pressure study

Four Medtronic insulin pumps and microtubules were fixed on a board. They were taken to 300 m in the Eureka Tower in Melbourne, Australia. The atmospheric pressure change was -22 mm Hg. The pump cartridges and microtubules were observed for bubble formation. The experiment was repeated three times.

Vibration study

Thirty Roche 3.15 mL cartridges were loaded with aspart insulin and then individually placed on a S.E.M. Vor-Mix agitator (S.E.M., Adelaide, Australia) for 10 s at 1500 rpm. The syringe was orientated horizontally (vibration force transverse across the syringe), vertically (vibration force longitudinally along the syringe), and in the center of the vortex machine (rotational force through the syringe). After each vibration event (10 s duration) the cartridges were examined for bubble formation.

RESULTS

Temperature study

When the cartridges were taken out of the refrigerator (4°C), placed into the pump at room temperature, and placed into an oven (37°C), bubble formation was

observed after the cartridges were removed from the insulin pumps. Bubbles were found in the 2 and 3.15 mL cartridges and in the tubing sets (see [figure 2](#)).

Pressure study

During the 300 m ascent, the pressure decreased by 22 mm Hg and bubble formation was observed in the pump cartridges and tubing.

Vibration study

Despite vigorously agitating the insulin pump cartridges, bubble formation was not observed in any cartridges or tubing.

DISCUSSION

We demonstrated bubble formation in the tubing and syringe of insulin pumps with an increase in temperature and a decrease in ambient pressure, but not with vibration.



Figure 2 Bubbles present in an insulin pump cartridge and line following an increase in temperature from 4°C to 37°C. The insulin cartridge and line containing aspart insulin was cooled to 4°C in a fridge and then moved to an oven at 37°C.

Henry's law predicts that bubbles will form as the temperature of the insulin rises.¹ In hot climates, it is recommended that insulin is refrigerated for storage.^{2,3} Often, the insulin is not warmed prior to use. This may result in bubble formation as the temperature of the insulin increases. The magnitude of temperature change required to produce bubble formation is currently unknown and would warrant further study. As ambient pressure decreases, Henry's law¹ predicts that bubbles will form. King *et al*⁴ have previously demonstrated that a 50 mm Hg decrease in ambient pressure causes bubble formation. A change in ambient pressure may occur in many situations, such as taking an elevator or driving up a hill and could potentially result in bubble formation. This study demonstrated that bubble formation can occur with a 22 mm Hg decrease in ambient pressure.

Vibration of an insulin pump may occur in many situations, such as when the insulin pump is dropped, driving on a rough road, or the pump is shaken. Our study did not demonstrate bubble formation as a result of vigorous vibration. Patients and their families may be reassured that dropping or shaking an insulin pump is unlikely to result in bubble formation. However, if there are bubbles already present in the syringe then vibration could move bubbles so they could enter the tubing.

It is currently unknown whether bubble formation in insulin pumps has any effect on insulin delivery by the pump. Temperature changes could be predicted to alter insulin delivery due to thermal expansion and contraction.⁵ Alterations in pressure could also be expected to result in changes in the rate of insulin delivery.⁶ King *et al*⁴ demonstrated that pressure changes during airline flight caused alterations in the rate of insulin delivery. Changes in insulin delivery due to environmental factors may occur independently of bubble formation. Such engineering principles are well known to insulin pump manufacturers, and modern insulin pumps have been designed to avoid changes in insulin delivery in response to known environmental phenomena. We anticipate that such design features would be common to all insulin pumps; however, we were unable to perform the temperature study, pressure study, and vibration study with insulin pumps from each manufacturer. Further studies are required to determine the effect of bubble formation on delivery of insulin across a range of insulin pumps.

Parents of children with type 1 diabetes often report feeling stressed. Insulin pump therapy has been associated with a reduction in parenting stress felt by carers of children with type 1 diabetes.⁷ Anecdotally, however, technical issues surrounding insulin pumps may be a source of anxiety. Technical difficulties with managing insulin pumps may lead to permanent cessation of insulin pump therapy.⁸ Patients and families are often concerned about the presence of bubbles as they fear non-delivery of insulin as the bubbles pass through the tubing. Currently, the impact of bubble formation on

insulin delivery is unknown. Advising patients and families about the causes of bubble formation may help them avoid bubble formation and assist with early identification. This may assist to reduce the already elevated anxiety levels of patients and families with type 1 diabetes.

Patients using insulin pump therapy should be aware of the potential for bubble formation in seemingly innocuous situations. Patients should be encouraged to warm refrigerated insulin to room temperature prior to use. If patients encounter an environment where there is a decrease in ambient pressure, inspection of the cartridge for bubble formation may be warranted. Patients and families can be reassured that vibration of an insulin pump is not likely to result in bubble formation. Further studies to determine the impact of bubble formation on insulin delivery are required to fully inform clinicians, patients, and families of the importance of bubble formation.

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Contributors BRK designed and coordinated the project, led the analysis, wrote the manuscript, and reviewed and edited the manuscript and is guarantor of the work included in the study. PEL, PWG, and GC collected and analysed data, wrote the manuscript, and reviewed and edited the manuscript.

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